COVID-19 Incidence Among Sixth Through Twelfth Grade Students by Vaccination Status

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Coronavirus disease 2019 (COVID-19), school closures, and quarantines have had substantial impacts on students' health and education.[1–3] Clinical trials have shown severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) vaccines to be safe and efficacious for adults, adolescents, and young children.[4] However, in some areas, vaccine uptake has been low among children and adolescents, especially compared with uptake in adults.[1] Additionally, real-world vaccine effectiveness data among adolescents and implications for in-person education are lacking. We investigated the impact of COVID-19 vaccination on SARS-CoV-2 incidence and within-school transmission in a cohort of sixth through twelfth grade students.

METHODS

We conducted a prospective cohort study of 1128 students (grades 6–12; ages 11–19) in a North Carolina private school from August 1, 2021 to November 12, 2021. During the 2020 to 2021 school year, the school employed a mask mandate and hybrid schedule, with only 2 documented occurrences of within-school transmission.

During the study period, the Centers for Disease Control and Prevention (CDC) classified SARS-CoV-2 county transmission as "high" and the delta variant comprised >99% of infections in the region.[5] The study period began on August 1, 2021 (day 0), when athletic activities and mandatory reporting of infections began. Full-time in-person classes began on August 17, 2021. Cumulative incidence of infection was assessed on November 12, 2021 (day 103).

School nurses monitored reporting of SARS-CoV-2 infections, symptoms, and exposures. Symptomatic persons were required to undergo SARS-CoV-2 testing; postexposure testing was encouraged, but not required. For reported infections, a nurse conducted case interviews and contact tracing using current CDC guidance and classified each infection as primary (resulting from community exposure) or secondary (resulting from within-school transmission).[6] Contacts who were vaccinated and/or had masked school exposure were not required to quarantine. School policy required universal masking indoors after August 9, 2021 and ventilation systems were upgraded with minimum efficiency reporting value 11 filters; high efficiency particulate air filters were not used. Physical distancing was minimal, and there was no routine surveillance testing for students or staff. At the time of data export, vaccination status had been confirmed with photo evidence of a completed series (2 doses) uploaded to an online portal.[7]

Deidentified data from case investigations and contact tracing were collected by school officials and provided to study investigators

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Mr Thakkar conceptualized and designed the study, drafted the initial manuscript, reviewed and revised the manuscript, designed the data collection instruments, collected data, and conducted the initial analyses; Drs Benjamin and Brookhart, and Ms Erickson reviewed and revised the manuscript; Drs Zimmerman and Kalu conceptualized and designed the study, coordinated, and supervised data collection, and critically reviewed the manuscript for important intellectual content; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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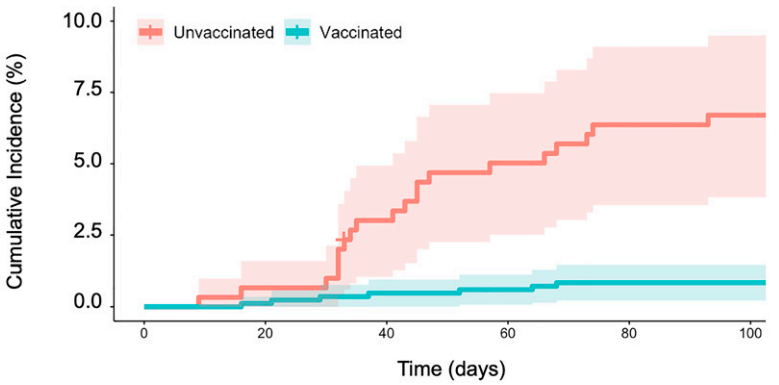
weekly. We computed descriptive statistics using R (version 4.1.0) and the *survival* package.[8] Cumulative incidence and 95% confidence intervals (95% CIs) were calculated using a Kaplan-Meier estimator. One participant, who was no longer enrolled at the school, was censored on day 33. Unadjusted vaccine effectiveness (VE) against documented SARS-CoV-2 infection and symptomatic infection was calculated as $(1 - \frac{\text{incidence among vaccinated}}{\text{incidence among unvaccinated}} \times 100\%)$. In calculating VE against symptomatic infection, students with asymptomatic infection were right-censored at time of infection. The Duke University Institutional Review Board (Pro00108129) determined this study to be exempt.



No. at risk (no. of events)						
Unvaccinated	299 (0)	297 (2)	289 (9)	283 (15)	279 (19)	278 (20)
Vaccinated	829 (0)	828 (1)	825 (4)	824 (5)	822 (7)	822 (7)

FIGURE 1
SARS-CoV-2 infection among sixth to twelfth grade students by vaccination status. Cumulative incidence of documented SARS-CoV-2 infection among sixth to twelfth grade students, by vaccination status. Day 0 was August 1, 2021. Shaded areas indicate 95% confidence intervals. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

RESULTS

As of November 2021, 829 (73.5%) students were vaccinated and 299 (26.5%) were unvaccinated, with each group contributing 84 953 and 29 572 person-days to the study, respectively. Demographic characteristics of the students are shown in Supplemental Table 2. Twenty (6.7%) unvaccinated students reported an infection during the study period, of which 16 (80%) were symptomatic. Seven (0.8%) vaccinated students reported an infection, of which 5 (71%) were symptomatic. Of the 27 infections, only 2 were classified as within-school transmissions, both resulting from unmasked exposures to unvaccinated index cases (Supplemental Table 2).

Unvaccinated students had 8.2 (95% CI, 3.5–19.4) times the incidence of documented infection and 9.2 (95% CI, 3.4–25.1) times the incidence of symptomatic infection compared with vaccinated students (Fig 1). Unadjusted VE was 87.8% (95% CI, 71.2%–94.8%) against documented infection and 89.1% (95% CI, 70.3%–96.0%) against symptomatic infection (Table 1). Due to varying vaccine eligibility in this group, a sensitivity analysis excluding sixth grade students indicated that there were no appreciable differences in the associations noted above (Supplemental Tables 3 and 4; Supplemental Fig 2).

DISCUSSION

Numerous studies have shown minimal secondary COVID-19 transmission in schools with mitigation measures.[9,10] Nevertheless, the implications of student vaccination rates on COVID-19 incidence and transmission have been minimally described. In this cohort of more than 1000 sixth to twelfth grade students, vaccine effectiveness against documented SARS-CoV-2 infection was 88%, providing evidence that vaccination is a critical component of safely continuing in-person education. This finding is comparable to other studies conducted when the delta variant was widespread.[1,3]

TABLE 1 SARS-CoV-2 Incidence and Vaccine Effectiveness Among Sixth to Twelfth Grade Students

	Number of Events	Total Person-Days at Risk	Incidence Rate per 1000 Person-Days	Incidence Rate Ratio (95% CI)	Vaccine Effectiveness,% (95% CI)
Documented SARS-CoV-2 infections[a]					
Unvaccinated	20	29 572	0.676	8.2 (3.5–19.4)	87.8 (71.2–94.8)
Vaccinated	7	84 953	0.082	Reference	
Symptomatic SARS-CoV-2 infections[b]					
Unvaccinated	16	29 572	0.541	9.2 (3.4–25.1)	89.1 (70.3–96.0)
Vaccinated	5	84 953	0.059	Reference	

CI, confidence interval; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
[a] Documented SARS-CoV-2 infection includes both symptomatic and asymptomatic infections.
[b] Students with asymptomatic SARS-CoV-2 infection were censored at time of infection.

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In this cohort, unvaccinated students had 8 times higher incidence of documented infection and less than 1% of vaccinated students reported an infection. As 1 primary infection can trigger a substantial number of quarantines, these findings indicate that vaccination may play a critical role in minimizing disease and keeping students in school; however, this may not be generalizable to other schools with lower vaccination rates. Our study also suggests that vaccination in conjunction with school-based mitigation measures may reduce within-school transmission; both documented school-related infections were the result of unmasked exposures to unvaccinated index cases.

Our study has some limitations. First, we relied upon self-reported vaccination status, which may have resulted in misclassification bias. Second, due to the nature of the data provided, we were unable to adjust VE estimates for covariates and confounders. Third, students with prior SARS-CoV-2 infection were not excluded from the study; if seropositivity was disparate among vaccinated participants and unvaccinated participants, VE may be biased. Fourth, asymptomatic infections may have been missed, due to the lack of regular asymptomatic testing. Finally, this study was conducted before the first cases of the omicron variant in North Carolina and included students from 1 urban private school, so the generalizability of the results may be somewhat limited.

In conclusion, in this real-world prospective cohort study of 1128 students, vaccinations substantially reduced SARS-CoV-2 incidence among adolescents and, along with other mitigation measures, kept students safely in-school during a variant-driven community surge.

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ABBREVIATIONS

CDC: the Centers for Disease Control and Prevention
CI: confidence interval
COVID-19: coronavirus disease 2019
IRR: incidence rate ratio
SARS-CoV-2: severe acute respiratory syndrome coronavirus 2
VE: vaccine effectiveness

CONFLICT OF INTEREST DISCLOSURES: Dr Kalu reports consultancy for IPEC Experts LLC. Dr Zimmerman reports funding from the National Institutes of Health (NIH) and US Food and Drug Administration (FDA). Dr Benjamin reports consultancy for Allergan, Melinta Therapeutics, Sun Pharma Advanced Research Co. Dr Brookhart serves on scientific advisory committees for American Academy of Allergy, Asthma & Immunology, AbbVie, Amgen, Atara Biotherapeutics, Brigham and Women's Hospital, Gilead, US Renal Data System, and Vertex; he receives consulting fees and owns equity in NoviSci and Target RWE. The remaining authors have no conflicts of interest to disclose.

REFERENCES

1. Naleway AL, Groom HC, Crawford PM, et al. Incidence of SARS-CoV-2 infection, emergency department visits, and hospitalizations because of COVID-19 among persons aged ≥12 years, by COVID-19 vaccination status — Oregon and Washington, July 4-September 25, 2021. *MMWR Morb Mortal Wkly Rep.* 2021;70(46):1608–1612
2. Hawrilenko M, Kroshus E, Tandon P, Christakis D. The association between school closures and child mental health during COVID-19. *JAMA Netw Open.* 2021;4(9):e2124092
3. Scobie HM, Johnson AG, Suthar AB, et al. Monitoring incidence of COVID-19 cases, hospitalizations, and deaths, by vaccination status — 13 U.S. jurisdictions, April 4-July 17, 2021. *MMWR Morb Mortal Wkly Rep.* 2021;70(37):1284–1290
4. Frenck RW Jr, Klein NP, Kitchin N, et al; C4591001 Clinical Trial Group. Safety, immunogenicity, and efficacy of the BNT162b2 COVID-19 vaccine in adolescents. *N Engl J Med.* 2021;385(3):239–250
5. Centers for Disease Control and Prevention (CDC). CDC COVID data tracker. Available at: https://covid.cdc.gov/covid-data-tracker/. Accessed December 7, 2021
6. Centers for Disease Control and Prevention (CDC). Considerations for case investigation and contact tracing in K-12 schools and institutions of higher education (IHEs). Available at: https://www.cdc.gov/coronavirus/2019-ncov/community/schools-childcare/contact-tracing.html. Accessed December 7, 2021
7. Magnus Health. COVID-19 school health tracking system. Available at: https://magnushealth.com/features/covid-19-health-tracking/. Accessed December 7, 2021
8. Therneau T. A Package for Survival Analysis in R. R package version 3.2-11. Available at: https://CRAN.R-project.org/package=survival. Accessed December 7, 2021
9. Boutzoukas AE, Zimmerman KO, Benjamin DK, et al. Secondary transmission of COVID-19 in K-12 schools: findings from two states. *Pediatrics.* 2022;149(12 Suppl 2)e2021054268K
10. Boutzoukas AE, Zimmerman KO, Benjamin DK Jr.; ABC Science Collaborative. School safety, masking, and the Delta variant. [published online ahead of print Oct 8, 2021]. *Pediatrics.* 2021;e2021054396

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